ORALS

Antiplatelet Agents

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TCT-1

Do Proton Pump Inhibitors Interact With Clopidogrel? Insights From ADAPT-DES

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Background: Selected proton pump inhibitors (PPI) interfere with clopidogrel metabolism, potentially attenuating P2Y12 receptor-based platelet inhibition. Previous observational and randomized trials have reported varying results regarding the clinical significance of this pharmacologic interaction. We examined this relationship in the large-scale, prospective Assessment of Dual Anti-Platelet Therapy with Drug-Eluting Stents (ADAPT-DES) study.
Methods: Platelet reactivity testing was performed using the VerifyNow point-of-care assay in 8,583 patients at 11 US and German sites after successful DES implantation. All patients were treated with aspirin and clopidogrel, and were followed for 1 year. PPI were prescribed at the discretion of treating physicians.
Results: At the time of the post-procedure P2Y12 test, 2,697 (31.4%) pts were on PPI, and 5,886 (68.6%) were not. Major baseline characteristics, P2Y12 results and 1-year events are summarized in the Table. The use of PPI was an independent predictor of higher platelet reactivity (HPR) units (PRU) in a linear regression model ($p<0.0001$), and additionally was independently associated with HPR as defined as PRU>208 (OR 1.38 [1.25, 1.52], p=0.0001). At discharge, 2,163 (25.2%) pts were prescribed PPI, and 6,419 (74.8%) were not. In propensity-adjusted proportional hazards regression models, PPI use was independently associated with out of hospital mortality (HR 1.52 [1.09, 2.12], p=0.01) and MACE (HR 1.23 [1.00, 1.51], p=0.049).

Baseline Characteristics	PPI (n=2437)	No PPI (n=6146)	p-value
Mean age, years	64.4 ± 10.7	63.3 ± 10.8	<0.0001
Diabetes	34.8%	31.3%	0.002
Hypertension	83.7%	77.8%	<0.0001
Acute coronary syndrome	57.5%	49.0%	<0.0001
VerifyNow P2Y12			
Mean PRU	201.9 ± 97.3	181.6 ± 95.8	<0.0001
PRU > 208	49.3%	39.7%	<0.0001
%inhibition	36.0 ± 27.7	41.8 ± 28.3	<0.0001
!-Year Follow-up (out of hospital)	PPI (n=2163)	No PPI (n=6419)	
Death	2.9%	1.5%	<0.0001
MI	2.1%	1.7%	0.26
MACE	6.9%	5.2%	0.004
Stent thrombosis (definite/probable)	1.1%	0.6%	0.05
Major Bleeding	5.3%	4.5%	0.11

Conclusions: In patients treated with clopidogrel after DES, the concomitant administration of PPI is associated with reduced platelet inhibition and adverse clinical outcomes. Additional studies are warranted to determine the risk-benefit ratio of PPI in patients after DES.

TCT-2

Comparative Effectiveness of Prasugrel vs. Clopidogrel Among Acute Myocardial Infarction Patients Treated With Percutaneous Coronary Intervention: 30-Day Outcomes from the TRANSLATE-ACS Observational Study

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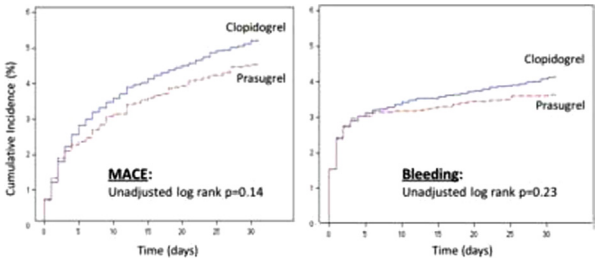
Background: Randomized trials have demonstrated the efficacy of prasugrel vs. clopidogrel in patients with acute MI, yet evidence of their effectiveness in real world practice is limited.
Methods: We studied use of prasugrel vs. clopidogrel among 11,417 STEMI and NSTEMI patients treated with PCI in the TRANSLATE-ACS study from 4/2010 to 10/2012. We used multivariable Cox models to compare 30-day MACE (death, recurrent MI, stroke, or unplanned revascularization) and any GUSTO defined bleeding.
Results: Prasugrel was used in 2,997 MI patients (26%) during PCI. Patients treated with prasugrel were younger (median 57 vs. 61 yrs), more likely to present with STEMI (59% vs. 49%), and less likely to have prior MI (15% vs. 21%) or diabetes (24% vs. 27%) than those receiving clopidogrel ($p<0.01$ for all). Prasugrel was used in 57 (9%) of patients with prior stroke/TIA, 64 (5%) over age 75, and 74 (14%) of patients <60 kg. Compared with clopidogrel, prasugrel was more often started during/after PCI, and used with bivalirudin or GPIIb/IIIa inhibitor. Unadjusted curves for 30-day MACE and bleeding diverged, but were not significantly different between prasugrel and clopidogrel treated patients (Figure). Multivariable analyses did not demonstrate significant differences in MACE (HR 0.96, 95%CI 0.79, 1.16) and bleeding (HR 1.04, 95%CI 0.77, 1.39).
Conclusions: While differences exist in patients receiving these drugs, the 30-day effectiveness and safety of prasugrel vs. clopidogrel were not significantly different in routine practice. Long-term outcomes comparisons are necessary and ongoing.



TCT-3

Outcomes in STEMI patients treated with clopidogrel or prasugrel: A propensity adjusted analysis from the INFUSE-AMI Trial

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Background: Prasugrel was superior to Clopidogrel in a large trial of acute coronary syndromes patients undergoing percutaneous coronary intervention (PCI) with heparin-based anticoagulation. It is not known whether more potent platelet inhibition with Prasugrel rather than Clopidogrel affects infarct size and clinical outcomes when primary PCI is performed with bivalirudin anticoagulation.